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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Francis Chi	Conf. no.: 4964
Serial No.:	10/516,428	Art Unit: 1644
Filed :	11/30/2004	Examiner: Michael E. Szperka
For :	ANTIBODIES TO ADIPOSE TISSUE	

Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

DECLARATION UNDER 37 CFR 1.132

Sir:

1. I, Tianshui Lu, am a Chinese citizen, residing in Hong Kong, and I am one of the listed inventors of the subject matter claimed in the above referenced application.

2. I have been involved in animal research since 1959, and am presently a Researcher at the laboratory of Animal Physiology and Biochemistry, at the College of Veterinary Medicine, at Naijing Agricultural University. My Curriculum Vitae is attached as Exhibit A to this declaration, and I make this Declaration in support of the patentability of our claimed invention. I have reviewed the office action dated January 16, 2008, and the cited patents, Flint (U.S. Patent No. 5,102,658, Cryer et al.(U.S. patent No. 5,367,054) and Lee (U.S. Patent No. 5,367,054).

3. Our invention is directed to " A method of reducing a content of adipose tissues in the body of a target animal using three animals, a source animal, an egg-laying farm animal and the target animal, the method comprising the steps of:

(i) preparing an antigen from adipose tissues of said source animal;

(ii) administering said antigen to said egg-laying farm animal;

(iii) allowing antibodies to be produced by said egg-laying farm animal in response to said antigen, thereby depositing said antibodies in eggs of said egg-laying farm animal;

(iv) obtaining egg yolk containing said antibodies from said eggs of said egg-laying farm animal;

(v) providing an ingestible composition including an amount of said egg yolk which contains an effective amount of said antibodies to said adipose tissue therein; and

(vi) orally administering the ingestible composition including said egg yolk to said target animal for ingestion... .". (As amended in the accompanying Amendment)

4. The Examiner has rejected claim 24 and the other dependent claims over three patents, Flint, U.S. patent no. 5,102,658 in view of Cryer, et al, U.S. patent no. 5,631,009, and in view of Lee, U.S. patent no. 5,367,054.

5. As the Examiner recognizes, Flint fails to describe that egg laying animals can be used to produce anti-adipocyte antibodies, nor does Flint disclose oral administration. Moreover, Flint fails to describe the preparation of an ingestible food composition, as a means of oral administration.

6. In my opinion, Flint is directed to the immunization of sheep with rat fat cell membranes. The animal source of the anti-rat adipocyte serum was essentially lamb blood, and isolation and purification steps were necessary to isolate the serum for administration by injection. One skilled in the art would be lead to believe that such steps are necessary to achieve a successful outcome. Certainly, one would not believe Flint to consider these steps optional, or easily dispensed with. Thus, Flint would lead a person skilled in the art away from the very simple, cost effective and easily practiced method of

our present invention.

7. The examiners' reliance on Cryer et al only further proves the novelty and non-obviousness of the present invention, as Cryer is also strictly concerned with the isolation and purification of Porcine adipocyte antigens, as illustrated in Claim 1:

"An isolated antigen present in the plasma membrane of mature porcine white adipocytes, which is not detectable in porcine liver, kidney, spleen, brain, cardiac muscle, skeletal muscle or lung or in porcine erythrocytes, which reacts with antisera raised against said adipocytes, said antigen being selected from the group consisting of a 37, 50, 51, and 121 KiloDaltons relative molecular mass antigen as determined by SDS-PAGE using markers of relative molecular mass 29, 45, 66, 97, 116, and 205 KiloDaltons." (Claim 1)

8. Cryer discusses research by Flint and found it lacking as follows:

"Although some of the above work has demonstrated experimentally the possibility of treating fat deposition in vivo by the administration of anti-adipocyte antibodies, it is a problem that the production of such antibodies may be very labour-intensive." (Col. 2, l. 1-5, Emphasis added)

9. Cryer proposes instead "The administration of the plasma membranes themselves as antigens could be considered, if they could be conjugated to carrier proteins and could thereby by made "non-self". However, the production of plasma membrane material from slaughterhouses poses difficulty of quality control. If the antigen(s) responsible for the fat reduction could be isolated and purified, the way would be open to making them by a recombinant DNA method or by protein synthesis." (Col. 2, l. 5-13, Emphasis added)

10. The invention presented by Cryer was described as follows:

"After considerable research, the inventors have isolated from porcine fat cell plasma membranes, antigens which appear to be specific to adipocytes (at least in the sense of not being detectable in many other body tissues of the animal) and reactive with antibodies to fat cell plasma membranes. (col. 2, l. 15-21)...The information given herein enables antigens to be identified, isolated and, by methods well known in the art, purified.(col. 3, l. 56-58) ...While either active or passive immunisation is likely to have an effect, active immunisation is preferred and for this purpose the antigen will have to be made "non-self" so that it does not suffer host immune tolerance. ....The favoured proposed route of administration for active immunisation is by subcutaneous injection." (Col. 4, l. 18-23, 32-33, Emphasis added)

11. Combining the teachings of Flint with Cryer, giving them a fair reading from the point of one skilled in that art, it is quite clear that isolation and purification are necessary steps to preparation of the isolate for administration by injection. Mentioning oral administration alone, without any proof of the capability is mere speculation. In fact, given the likely degradation when passing through the digestive system, one would not expect oral administration to be particularly effective. Certainly, given the emphasis on purification and injection, one skilled in the art would not be lead to the ingestible composition of the present invention. To the contrary, combining Flint and Cryer leads one to believe that it is necessary to first isolate and purify the material before administration, preferably by injection, as both Flint and Cryer propose.

12. Adding Lee simply describes other purification steps, here of eggs, but still with quite labor intensive steps. Just as discussed in Cryer, lee suffers as "the production of such antibodies may be very labour-intensive" and of course, quite costly to perform as well.

13. Lee discusses the isolation and purification steps as follows:

"The present invention is directed toward a method for purification of immunoglobulin egg yolk, including the steps of extracting the egg yolk immunoglobulin using medium-chain fatty acids including, for example, caprylic acid, to obtain an immunoglobulin-containing aqueous phase, followed by the steps of subjecting the aqueous phase to ion-exchange chromatography, for example, anion exchange chromatography; subjecting the recovered immunoglobulin fraction to additional ion-exchange chromatography, for example, cation exchange chromatography; subjecting the recovered immunoglobulin to protein precipitation, e.g., ammonium sulfate precipitation; and subjecting the recovered immunoglobulin to gel filtration and/or de-salting by dialysis or diafiltration. (Col. 3, l. 58-col. 4, l. 4, Emphasis added)

14. It is difficult to find anything in these three patents which would lead one skilled in the art to the present invention. To the contrary, they lead one away from, not toward the present invention, and so one skilled in that art would not find the present invention to be obvious. Rather they would be quite surprised that a low cost, simply, high volume production of an ingestible composition, that can be added to a standard animal feed for ease in administration could actually work.

15. I believe the inventive method and animal feed as presented in the claims of our patent application are distinguishable from the prior art as the cited patents lead one away from the particular steps of:

"(iii) allowing antibodies to be produced by said egg-laying farm animal in response to said antigen, thereby depositing said antibodies in eggs of said egg-laying farm animal;

(iv) obtaining egg yolk containing said antibodies from said eggs of said egg-laying farm animal;

(v) providing an ingestible composition including an amount of said egg yolk which contains an effective amount of said antibodies to said adipose tissue therein; and

(vi) orally administering the ingestible composition including said egg yolk to said target animal for ingestion... .".

I, the undersigned inventor further declare that all statements herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further, and that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Inventor's Signature Tianshui Lu.

Tianshui Lu, co-inventor

Date: APR. 04. 2008

2.5.10

Curriculum Vitae

Name
Tianshui Lu

Date of birth
October 2,1936

Foreign language
English & Russia

Education
Major of Farming, Department of Farmingand Veterinary Medicine
Nanjing Agricultural College.

Work experience

1994.1-present	Researcher at Laboratory of Animal Physiology and Biochemistry, College of Veterinary Medicine, Naijing Agricultural University .
1992-1996	Graduate Student Supervisor in Nanjing Agriculture University.
1989.10-1999.11	Director at Council of Feeding and Feed, Association of Jiangsu Milk Cow.
1987.10-present	Secretary-general at Branch of Animal Physiology and Biochemistry, Acda of Farming and Veterinary Medicine in China.
1986.4-1994.1	Associate researcher in Nanjing Agricultural Univerisity.
1985.11-1986.5	Visiting scientist at Department of Farming, College of life science, Cornell University, USA.
1984.3-1986.3	Deputy Director at Department of Veterinary Medicine, Nanjing Agriculture University.
1978.3-1986.4	Instructor at teaching and research group of physiology, Department of Farming and Veterinary Medicine, Nanjing Agricultural College.
1959.12-1978.3	Teaching Assistant at teaching and research group of physiology, Department of Farming and Veterinary Medicine, Nanjing Agricultural College.

Research Areas

Animal Physiology (digestion/lactation physiology) & Feed Nutrition and Feed Additive

Research harvest

1. Physiology study of fibrin of digestion and improvement in large intestine of porcine. – Class 4 Prize of science committee of province in 1978
2. Research of non-common diet in regulating rumen metabolism to increase feed utilization in ruminant livestock – Class 3 Prize of agricultural science and technology advancement in 1986.
3. Research of improvement of digestion & metabolism in dairy cattle to increase feed utilization & product capability. – Class 3 Prize of agricultural science and technology advancement in 1991.
4. Selection and breeding of core troop of China black white dairy cow. – Class 3 Prize of Agricultural ministry in 1992.
5. Technical approach of all-around utilization about agricultural resource in Ning Zhen Yang hill. – Class 3 Prize of Jiangsu province in 1992.
6. Research of Cysteamine in regulating somatostatin to accelerate Animals Growth. – Class 3 Prize of science and technology of national educational committee in 1995.
7. Research & development of carboxyl-methyl-urea (non-protein nitrogen feed additive). – Class 1 Prize of Nanjing Agricultural University.
8. Mechanism of Daidzein in increasing male livestock product capability.
9. Basic theory of increased meat quality livestock & poultry. – Prize 2 of science and technology advancement in ministry of education in 1998.
10. New technology of accelerating Animal Growth. –National Invention Patent (ZL91108266.2) in 1994.
11. New technology of accelerating poultry to end embrace. -- National Invention Patent (ZL91108266.2) in 1996.

Works

Science of China Buffalo (take part in writing: $P_{178-206}$, $P_{412-446}$)
Scientific and technical publishing company, 2000.12

Major Thesis

1. Some traits of lactation physiology in the offspring (F_1) of Holand male milk cattle and female Yak. Farming and Veterinary Medicine. 1480.NO.5.4-8
2. Traits of lactation physiology in 犏牛 Nanjing Agricultural University Transaction. 1980.NO.2.1-7
3. Changes of rumen PH, levels of ammoniac nitrogen and protein in goats at three different feed mode. Nanjing Agricultural University

Transaction. 1982.NO.3.118-124

4. Study of rumen digestion and metabolism in buffalo IV Effects of adding urea, ammonia sulfate in rice grass on serum metabolism in winter. Nanjing Agricultural University Transaction. 1984.NO.3.88-95
5. Some traits of lactation physiology in Molanili and the offspring of it & buffalo. Nanjing Agricultural University Transaction. 1989, 12(2): 86-90
6. Experiment of using carboxyl-methyl-urea instead of part of bean cake in the high-product milk cow diet. Farming and Veterinary Medicine. 1989 NO.3 110-111
7. Physiological changes of lactation and physiological regulation to improve lactation capability during improvement-breeding of yellow cattle, buffalo and Yak. Farming and Veterinary Medicine. 1989 NO.5 196-198
8. Changes of serum levels of hormones during buffalo lactation induced by hormones. Nanjing Agricultural University Transaction. 1990, 13(1): 98-101
9. Elementary study of milking with machine in buffalo. Nanjing Agricultural University Transaction. 1992, 15(1): 97-102
10. Changes of serum oxytocin and mamma internal pressure during lactating reflex in buffalo. Nanjing Agricultural University Transaction. 1993, 16(1): 91-95
11. Development of growth hormone and galactophore herbivore livestock 1994 NO.2 13-14